

Please amend the application as follows:

In the claims:

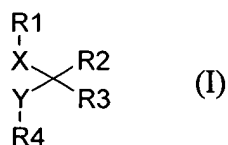
This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Canceled)

2. (Previously presented) A formulation comprising:

(i) an inhibitor of carboxypeptidase U or a pharmaceutically acceptable salt thereof; and

(ii) a thrombin inhibitor or a derivative thereof,
in admixture with a pharmaceutically acceptable adjuvant,
diluent, or carrier, wherein the inhibitor of carboxypeptidase U is a compound of formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R₁ is selected from the group consisting of:

C₁-C₆ alkyl, substituted with one or more basic groups;

cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom;

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

and

aryl, substituted with one or more basic groups;

R₂ is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, nitro, thiol, a Z₂N-CO-O- group, a ZO-CO-NZ- group, and a Z₂N-CO-NZ- group;

R₃ is selected from the group consisting of COOR₅, SO(OR₅), SO₃R₅, P=O(OR₅)₂, B(OR₅)₂, P=OR₅(OR₅), tetrazole, and a carboxylic acid isostere;

R₄ is SH, S-CO-C₁-C₆ alkyl, or S-CO-aryl;

R₅ is H, C₁-C₆ alkyl, or aryl;

R₆ is H or C₁-C₆ alkyl;

X is selected from the group consisting of O, S, SO, SO₂, C(Z)₂, N(Z), NR₆SO₂, SO₂NR₆, NR₆CO, and CONR₆;

Y is C(Z)₂; and

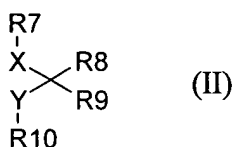
Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, cycloalkyl and heterocyclyl.

3. (Previously presented) A formulation comprising:

(i) an inhibitor of carboxypeptidase U or a pharmaceutically acceptable salt thereof; and

(ii) a thrombin inhibitor or a derivative thereof,

in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier, wherein the inhibitor of carboxypeptidase U is a compound of formula II,



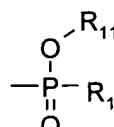
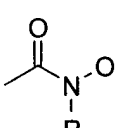
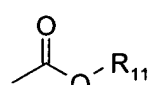
or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein:

R₇ is selected from the group consisting of:

C₁-C₆ alkyl, substituted with one or more basic groups;
cycloalkyl, substituted with one or more basic groups;
heterocyclyl, comprising at least one nitrogen atom;
heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups; and
aryl, substituted with one or more basic groups;

R₈ is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, nitro, thiol, Z₂N-CO-O-, ZO-CO-NZ-, and Z₂N-CO-NZ-;

R₉ is selected from the group consisting of COOR₁₁, SO(OR₁₁), SO₃R₁₁, P=O(OR₁₁)₂, B(OR₁₁)₂, P=OR₁₁(OR₁₁), tetrazole, and a carboxylic acid isostere;

R₁₀ represents a -group, or a -group, or a -group,

R₁₁ is H, C₁-C₆ alkyl, or aryl;

R₁₂ is C₁-C₆ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

H₂N-C(Z)-CONH-C(Z)- or H₂N-C(Z)- group;

R₁₃ is H or C₁-C₆ alkyl;

X is selected from the group consisting of O, S, SO, SO₂, C(Z)₂, N(Z), NR₁₃SO₂, SO₂NR₁₃, NR₁₃CO, and CONR₁₃;

Y is selected from the group consisting of O, N(Z), S, C(Z)₂, and a single bond; and

Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, cycloalkyl, and heterocyclyl, with the proviso that when X is O, S, SO, SO₂, N(Z), NR₇SO₂, SO₂NR₇, or NR₇CO, then Y is C(Z)₂ or a single bond.

4. (Previously presented) The formulation according to claim 2 or 3, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

5. (Previously presented) The formulation according to claim 4, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

6. (Previously presented) The formulation according to claim 5, wherein the low molecular weight thrombin inhibitor is HOOC-CH₂-(R)Cgl-Aze-Pab-H or a prodrug thereof.

7. (Previously presented) The formulation according to claim 6, wherein the prodrug is EtOOC-CH₂-(R)Cgl-Aze-Pab-OH.

8. (Previously presented) The formulation according to claim 2 or 3, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

9. (Currently amended) A kit of parts comprising:
(i) a vessel comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof;
(ii) a vessel comprising a thrombin inhibitor, or a derivative thereof; and

(iii) instructions for the sequential, separate or simultaneous administration of the inhibitors (i) and (ii) to a patient in need thereof, wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

10. (Canceled)

11. (Previously presented) The kit of parts according to claim 9, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

12. (Original) The kit of parts according to claim 11, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

13. (Original) The kit of parts according to claim 12, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

14. (Original) The kit of parts according to claim 13, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

15. (Previously presented) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

16. (Currently amended) A kit of parts comprising:
(i) a ~~pharmaceutical~~ formulation comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt

thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
(ii) a ~~pharmaceutical~~ formulation comprising a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier, wherein inhibitors (i) and (ii) are each formulated for administration in conjunction with the other, and wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

17. (Previously presented) The kit of parts according to claim 16, wherein inhibitors (i) and (ii) are formulated for sequential, separate or simultaneous administration.

18. (Canceled)

19. (Currently amended) The kit of parts according to claim 16 ~~or 17~~, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

20. (Original) The kit of parts according to claim 19, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

21. (Original) The kit of parts according to claim 20, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

22. (Original) The kit of parts according to claim 21, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

23. (Previously presented) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

24. (Canceled)

25. (Currently amended) A method for the treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

(i) an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and

(ii) a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier, wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

26. (Previously presented) The method according to claim 25, wherein the administration of inhibitors (i) and (ii) is sequential, separate or simultaneous.

27. (Canceled)

28. (Currently amended) The method according to claim 25 ~~or 26~~, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

29. (Previously presented) The method according to claim 28, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

30. (Previously presented) The method according to claim 29, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

31. (Original) The method according to claim 30, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

32. (Currently amended) The method according to claim 25 ~~or 26~~, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

33. (Previously presented) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired, which method comprises administering to the patient a formulation according to claim 2 or 3.

34-40. (Canceled)

41. (Previously presented) The formulation according to claim 2 or 3, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.

42. (Previously presented) The formulation according to claim 2 or 3, wherein the molar ratio between the inhibitor of

carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.

43-46. (Canceled)

47. (Previously presented) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 50:1 to 1:50.

48-53. (Canceled)

54. (Previously presented) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.

55-60. (Canceled)

61. (Previously presented) The method according to claim 25, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.

62. (Canceled)

63. (Canceled)